

**Remarks**

This application has been carefully reviewed in light of the Office Action mailed November 4, 2004. Claims 1-34 are pending and stand rejected. Reconsideration and allowance of Claims 1-34 is respectfully requested in view of the following remarks.

**Rejections Under 35 U.S.C. § 102**

The Office Action rejects Claims 1-34 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent 5,699,798 to Hochman, et al. (“Hochman”). Applicants respectfully traverse.

Claim 11 recites “selecting a fluorescent contrast agent as a function of a predetermined time-of-flight for a tissue to be imaged in accordance with a mathematical expression modeling the behavior of multiply scattered light traveling through the tissue, the fluorescent contrast agent having a fluorescent lifetime within a factor of ten of the predetermined time-of-flight.” The Office Action asserts that this limitation is disclosed in *Hochman* with no explanation other than the citation of Col. 3, Ln. 22; Col. 4, Ln. 12; Col. 5, Lns. 39-59, and Col. 9, Lns. 37-60, portions that do not disclose the above claim language.

Applicants respectfully submit that *Hochman* does not disclose the above-identified claim language. Specifically, *Hochman* makes no mention of “selecting a fluorescent contrast agent as a fraction of a predetermined time-of-flight for a tissue to be imaged” or that the selection is “in accordance with a mathematical expression modeling the behavior of multiply scattered light traveling through the tissue.” Indeed, the phrases “predetermined time-of-flight” and multiply scattered light do not appear in *Hochman*, nor has the Office Action identified any act within *Hochman* allegedly meeting this claim language. There is none. For at least this reason, Claim 11 is allowable, as are the claims depending therefrom. Independent Claims 1, 17 and 23 are allowable for analogous reasons, as are the claims depending therefrom. Reconsideration and favorable action are requested.

For the convenience of the Examiner, an analogy is provided below to the science and mathematics behind a relationship between the time-of-flight and the fluorescent life times. It is emphasized that this description is provided to facilitate an understanding of such a relationship and is not intended to be a completely accurate description of the operation of the invention, and does not limit the invention of Claim 11. The detection of the multiply scattering light may be thought of as analogous to detecting light from a series of progressively dimmer light bulbs lined up along the line of sight of a detector such that the

detector can only see the first light bulb in the line. This is analogous to detecting fluorescence at the tissue surface that is generated from deeper and deeper tissue regions. Because excitation light exponentially attenuates as it propagates deep into the tissue, the strength of the fluorescent "source" or light bulb also becomes exponentially weaker with increased distance inside the tissue from the surface of the illuminated tissue. As excitation light propagates and attenuates during its travel deep into the tissue, it therefore turns on the closest light bulb at the surface, say a 10Watt bulb, and successively lower wattage bulbs, 0.1 Watt, 1 microWatt, etc. as the excitation light propagates in time away from the tissue surface.

Consider the case of short-lifetimes, such that the photon migration times (or the time it reaches for excitation light to travel deep into the tissue) are longer than the fluorophore lifetime or the time of which the light bulbs are turned off. When the first light bulb is turned off (as could be the case with a short-lived fluorophore), then the second, dimmer-bulb may be seen. In this analogy, the light bulbs correspond roughly to the fluorescent contrast agent. Thus, to detect multiply scattered fluorescent light deep within a tissue, the "light bulbs" in the front of the line need to fluoresce, but then need to turn off quickly enough such that the "light bulbs" in the back of the line may also be seen before they turn off. Conversely, if the fluorescent lifetime is long in comparison to the photon "time-of-flight" than the 10W bulb will "swamp" out the small amount of light from the deeper and dimmer bulbs and consequently, not enabling them to be seen. This example corresponds roughly to a desirable relationship between the fluorescent lifetime of the agent and the mean time of flight of the scattering light.

Indeed, Figures 17A and B of the present application show that the change in measurement variable (phase and modulation ratio) change as a function of fluorescent target position when the fluorescent lifetimes are smaller than or within the same order of magnitude of photon "time-of-flight" but that such changes disappear when the lifetime is much larger than the photon "time-of-flight." Figures 17-20 directly show mathematical predictions and experimental measurements. The present invention recognizes — and the present specification describes — the derivation of desirable relationships between this time of flight and the fluorescent lifetime.

In addition to being allowable for the reasons described above, all claims are also allowable because *Hochman* does not disclose the use of multiply scattering light, nor has the

Office Action identified any component of *Hochman* allegedly corresponding to such multiply scattering light. The concept of the use of multiply scattering light is described in detail in the present specification, and a physical analogy was described above in the context of the lifetime of a fluorescent agent. Upon review of these passages, it should be clear that *Hochman* does not utilize multiply scattering light. For at least this additional reason, all claims are allowable. Reconsideration and favorable action are requested.

Conclusion

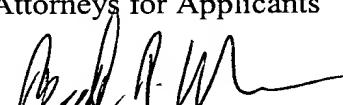
Applicants have now made an earnest attempt to place this case in condition for immediate allowance. For the foregoing reasons and for other apparent reasons, Applicants respectfully request allowance of all pending claims.

If the Examiner feels that prosecution of the present Application may be advanced in any way by a telephone conference, the Examiner is invited to contact the undersigned attorney at 214-953-6447.

Applicants do not believe that any fees are due. However, the Commissioner is hereby authorized to charge any fees or credit any overpayments to Deposit Account No. 02-0384 of Baker Botts L.L.P.

Respectfully submitted,

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